ESSENTIALS OF GLYCOBIOLOGY

Lecture 30

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FREE GLYCANS AND THEIR ROLES AS SIGNALING MOLECULES

LECTURE OUTLINE

- **Background**
- **Oligosaccharide signals trigger the initiation of the plant defense response**
- **Nod factor signals initiate the nitrogen-fixing *Rhizobium*-legume symbiosis**
- **Chitin oligosaccharide signals in plant defense and early animal development**
- **Other oligosaccharide signals in early plant and animal development**
- **Pattern recognition receptors and innate immunity**

•Background:

Potential of oligosaccharides as signals:

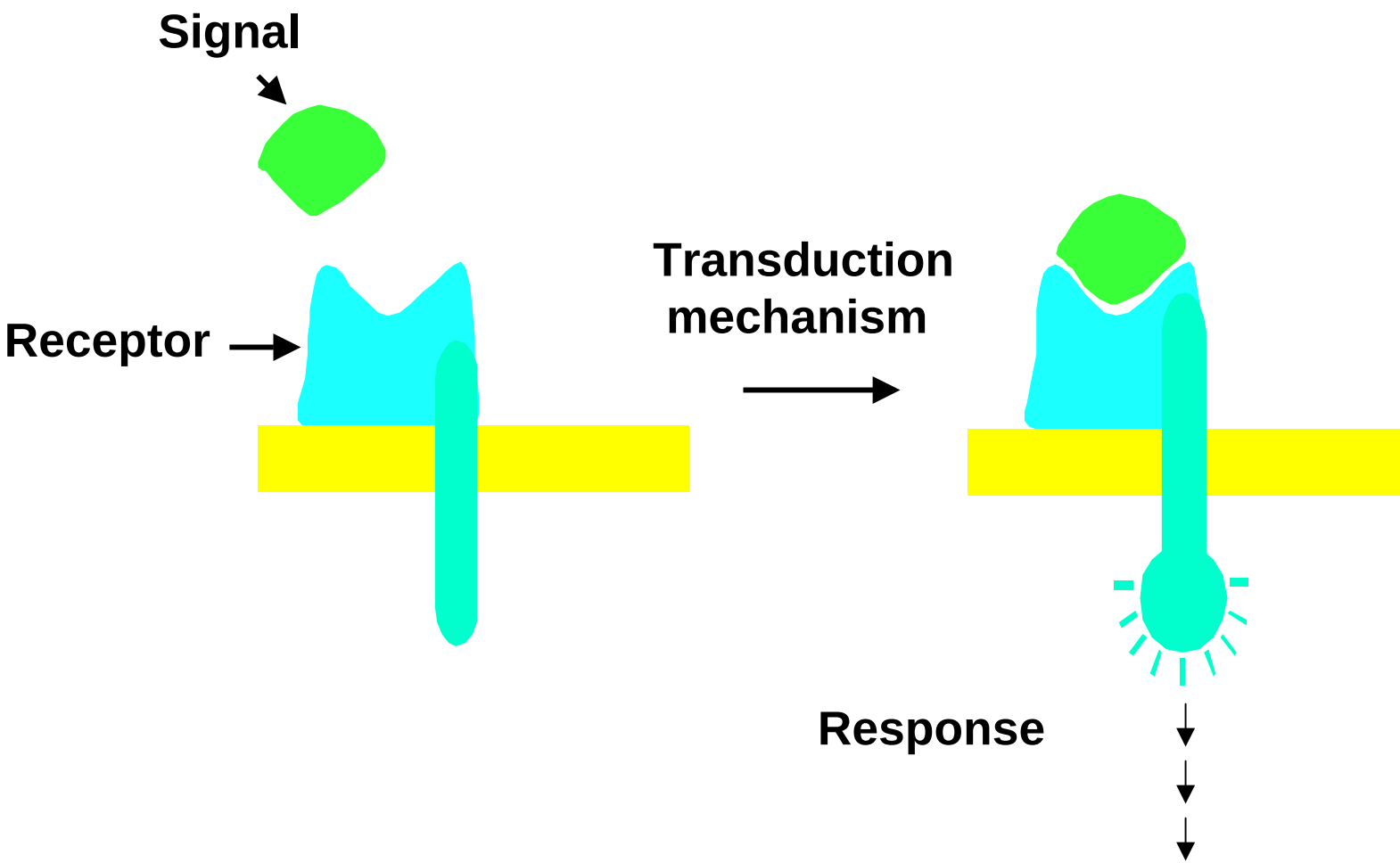
1) Variety of linkages between monomers enables a large number of conformational variations.

Portion of Table shown in Lecture 1:

Macromolecule	Building block	Possible variations in a trimer
Protein	Amino acids	6
Nucleic Acid	Nucleotides	6
Carbohydrate	Hexoses	1,056 to 27,648

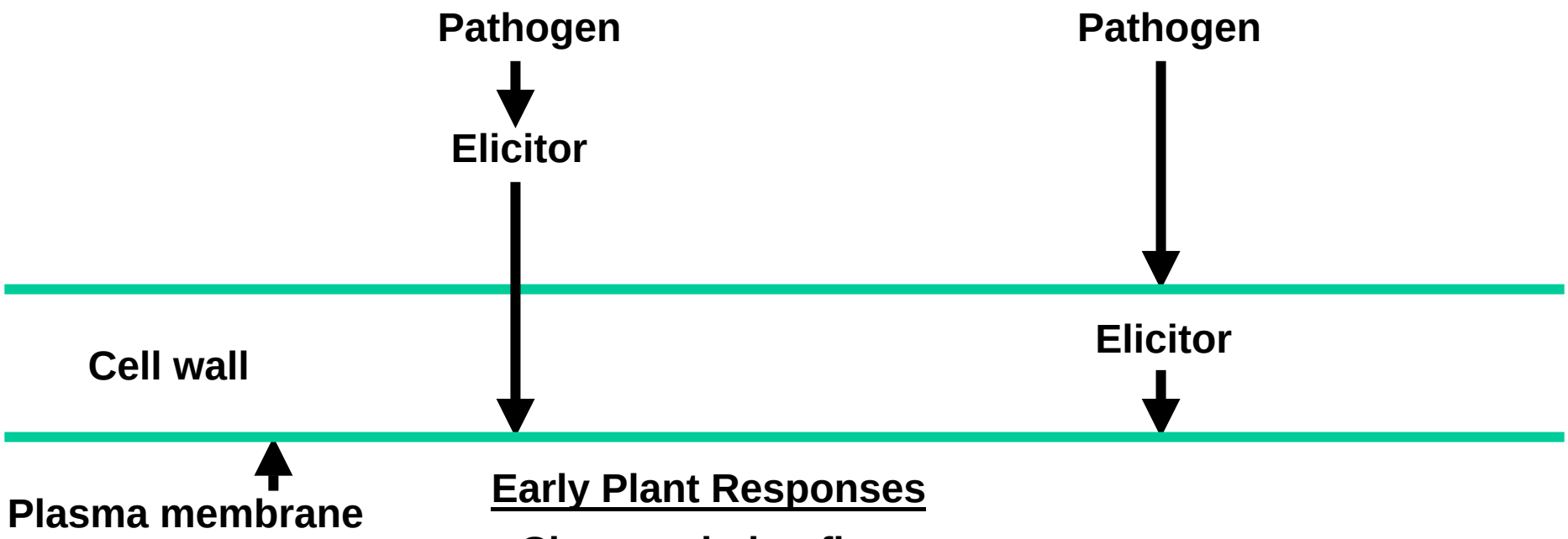
2) Many hydroxyls available for modification.

Basic elements of signaling system:



- **Oligosaccharide Signals Trigger the Initiation of the Plant Defense Response**

Plant Defense Responses:



Early Plant Responses

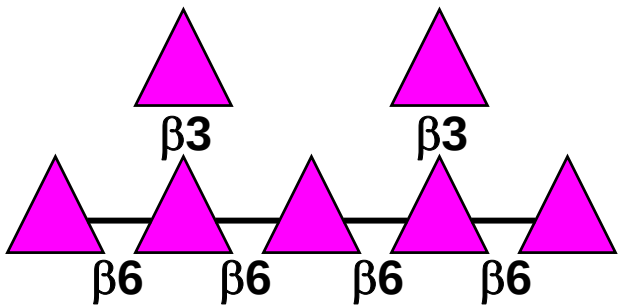
Changes in ion fluxes
Oxidative burst → H_2O_2 and O_2^-
Activation of early defense-related genes
Phytoalexin production
Structural changes in cell walls

The first oligosaccharide signal was identified in the fungus, *Phytophthora megasperma*, a fungal pathogen of soybean.

Isolated from cell walls

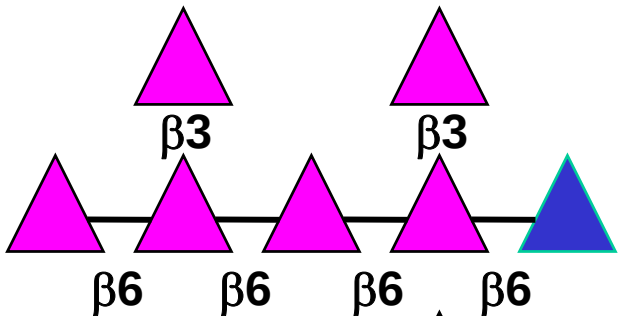
Elicits phytoalexin production in soybean seedlings

Structure confirmed by chemical synthesis

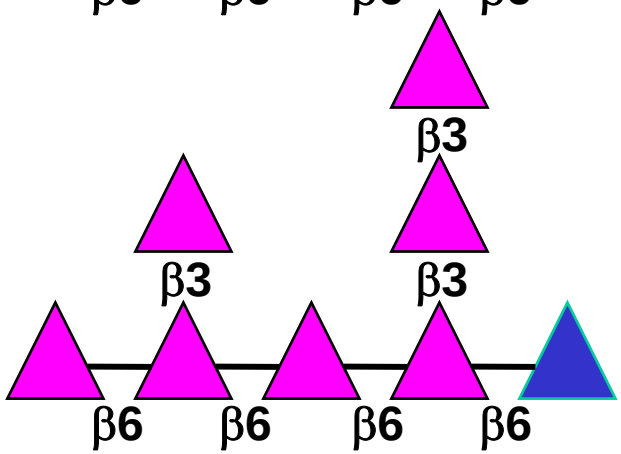


Hepta-β-glucoside

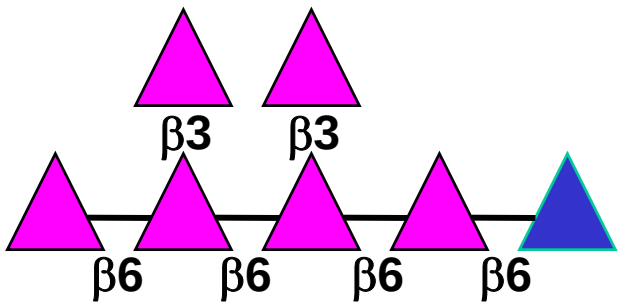
Relative Activities of Oligo-β-Glucosides



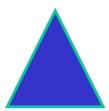
Relative Elicitor Activity	Relative Binding Activity
1000	1000



Relative Elicitor Activity	Relative Binding Activity
270	93

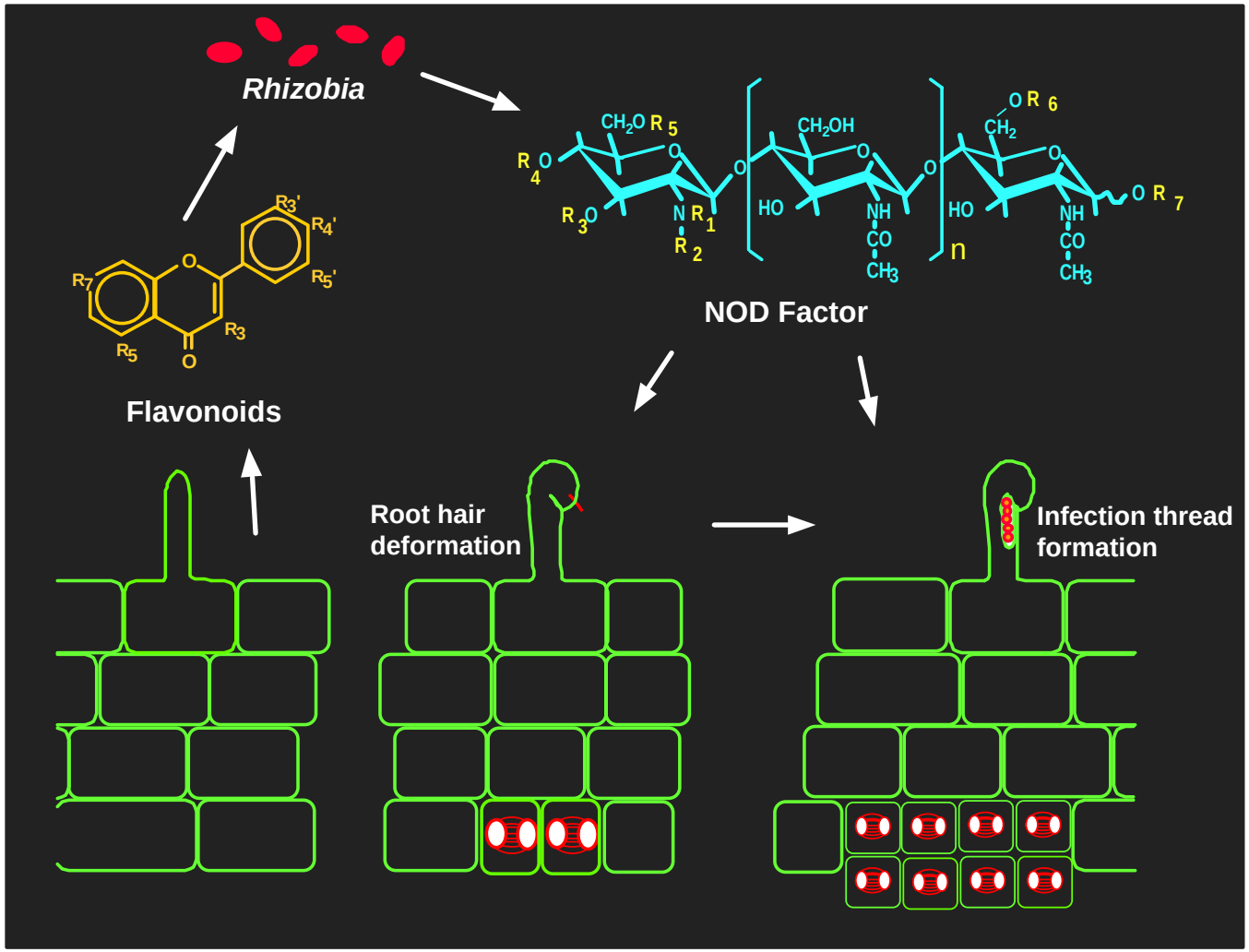


Relative Elicitor Activity	Relative Binding Activity
1.2	1.3

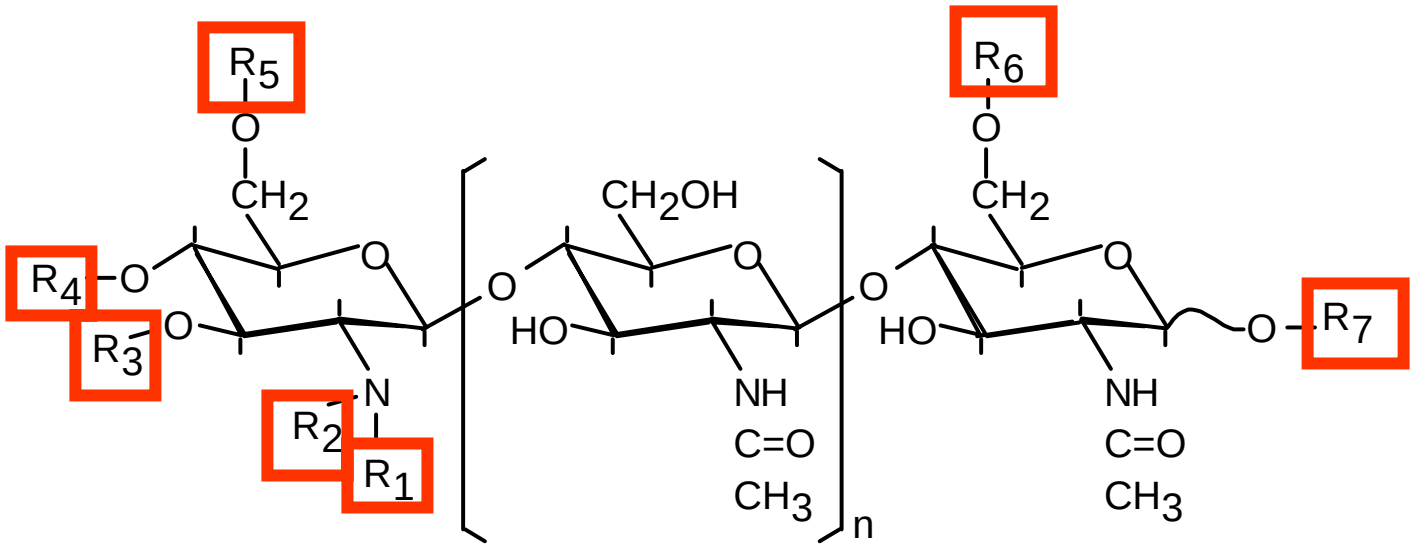


= reduced glucose

- **Nod factor signals initiate the nitrogen-fixing *Rhizobium*-legume symbiosis**



GENERIC STRUCTURE OF NOD FACTORS



R_1 = H, Methyl

R_2 = C16:2, C16:3
C18:1, C18:3, C18:4
C20:3, C20:4

R_3 = H, Cb

R_4 = H, Cb

R_5 = H, Ac

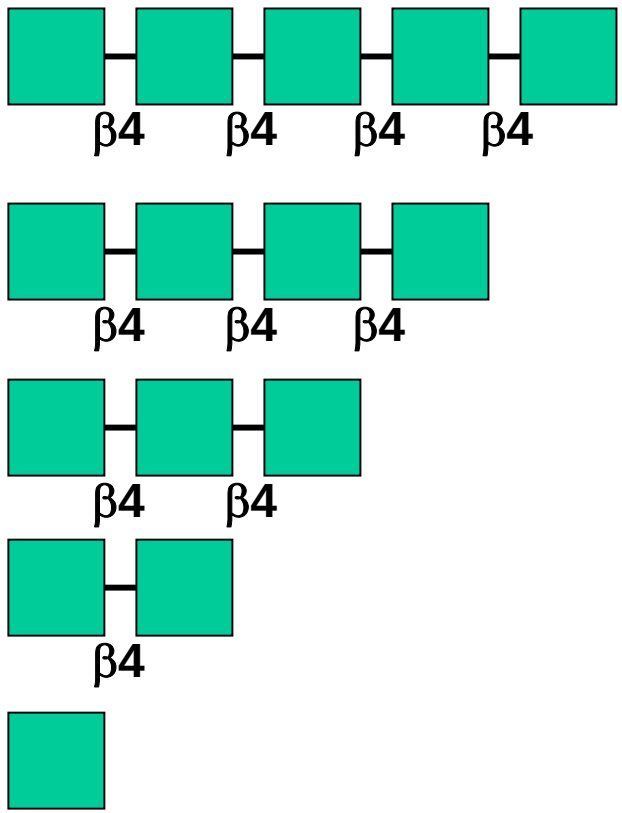
R_6 = H, Ac,
SO_4
Fuc
AcFuc
MeFuc

R_7 = H
Glycerol

n = 1 - 4

- **Chitin oligosaccharide signals in plant defense and early animal development**

Elicit alkalinization of medium of tomato cell cultures



	Biological activity (nanomolar)
	0.1
	0.1
	50
	100,000
	>1,000,000

Evidence for chitin oligosaccharide signaling in early animal development:

In *Xenopus laevis* the developmentally regulated protein, DG42, is homologous to Nod C, the enzyme that synthesizes the chitin backbone of the Nod factors in rhizobia.

DG42 is only expressed between the gastrula and neurulaation stages.

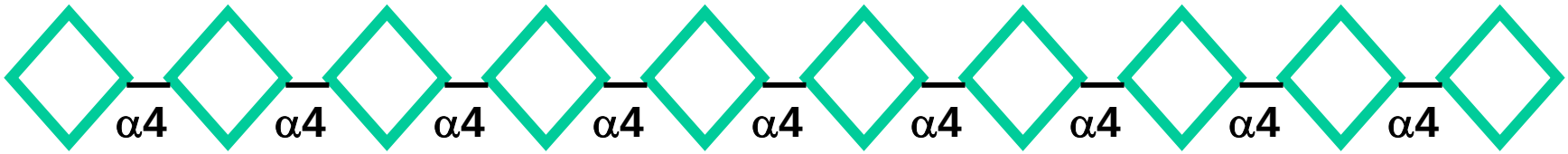
DG42 can direct the synthesis of chitin oligosaccharides *in vitro.*

Chitin oligosaccharides can be synthesized by extracts of gastrulation stage embryos of cyprinid fishes (zebra fish and carp).

Microinjection of fertilized eggs with antibodies against DG42 leads to severe defects in trunk and tail development.

- **Other oligosaccharide signals in early plant and animal development**

Oligogalacturonides - isolated from plant cell walls



Serve as signals in both defense and in plant development

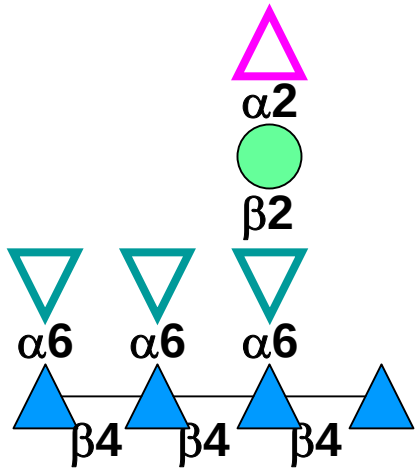
DEFENSE: Usually need DP of 10-14 to elicit phytoalexin accumulation.

DEVELOPMENT: Different DP elicit different responses.

= Galacturonic acid

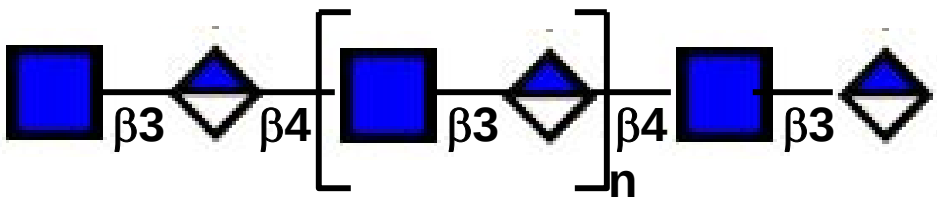
DP = degree of polymerization

Xyloglucan nonasaccharide:



Concentrations of 10^{-8} M inhibit auxin-induced elongation of stem fragments.

Hyaluronan fragments:



Activate antigen presenting cells and other proinflammatory responses, signal cell motility and adhesion

- **Innate immunity**

Dependent on proteins and phagocytic cells that recognize conserved features of pathogens that are absent in the host.

Found in vertebrates, invertebrates and plants.

Pattern recognition receptors

Recognize pathogen-associated immunostimulants

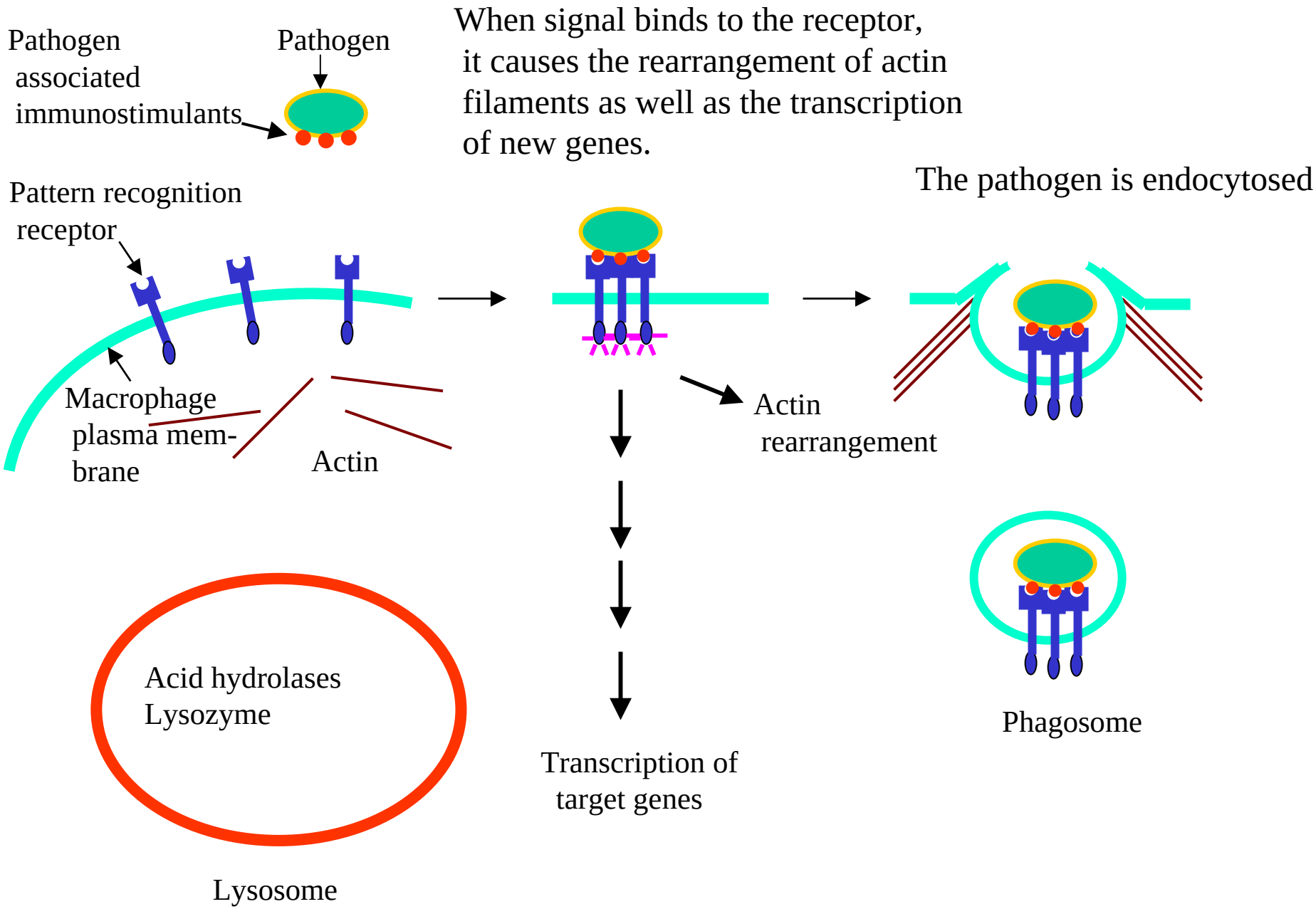
Examples of repeating patterns that often occur on pathogen surfaces

Chitin, glucan and other polysaccharides in cell walls of fungi

Peptidoglycan cell wall and flagella of bacteria

Lipopolysaccharide on Gram-negative bacteria

Teichoic acids on Gram-positive bacteria


Pathogen associated immunostimulants
Pathogen
When signal binds to the receptor, it causes the rearrangement of actin filaments as well as the transcription of new genes.
The pathogen is endocytosed
Pattern recognition receptor
Macrophage plasma mem-brane
Actin
Actin rearrangement
Acid hydrolases
Lysozyme
Lysosome
Transcription of target genes
Phagosome